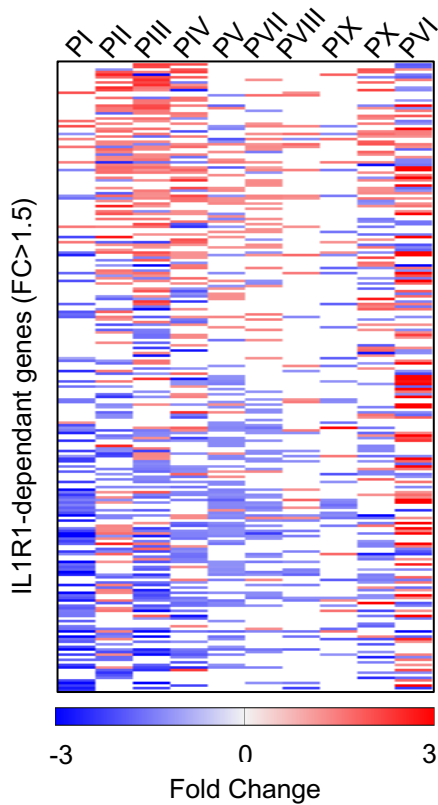


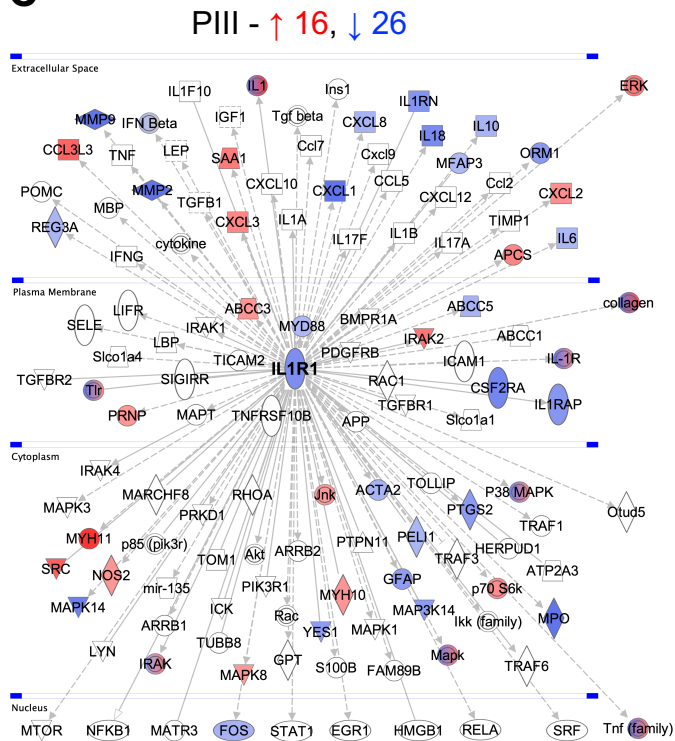
Supplementary Figure 1. Urine Substance P levels prior to treatment in patients and study controls.

Urine Substance P levels were measured by ELISA in patients with bladder pain syndrome ($n = 16$) other urological diagnoses ($n = 4$) and compared to healthy controls without urological morbidity ($n = 6$). The data was analyzed by Kruskal-Wallis with Dunn's correction. n.s. = not significant. The control patient with cystitis cystica had elevated SP levels and responded to IL-1RA treatment.

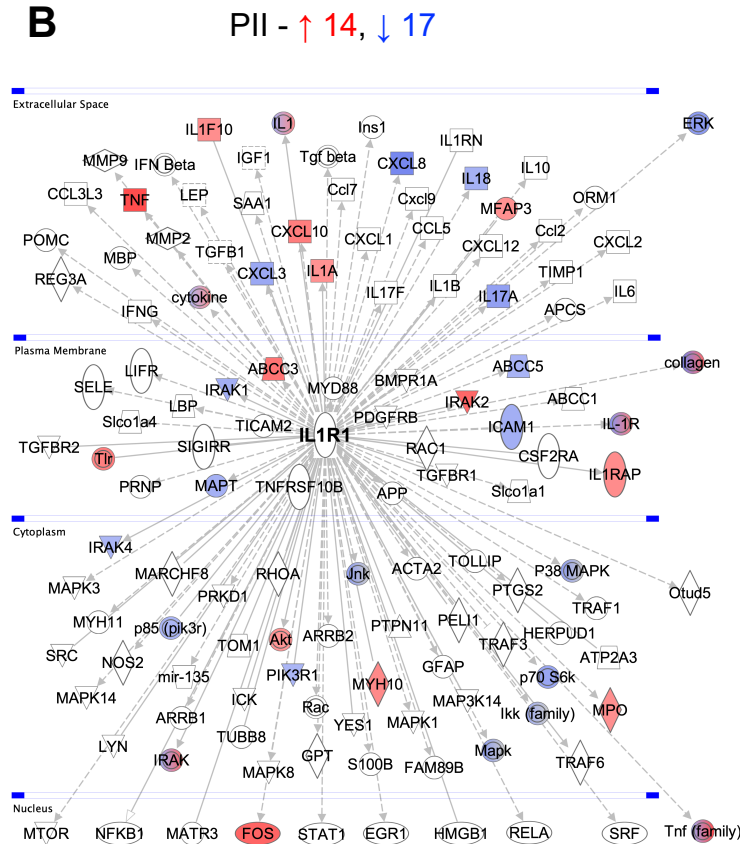
A



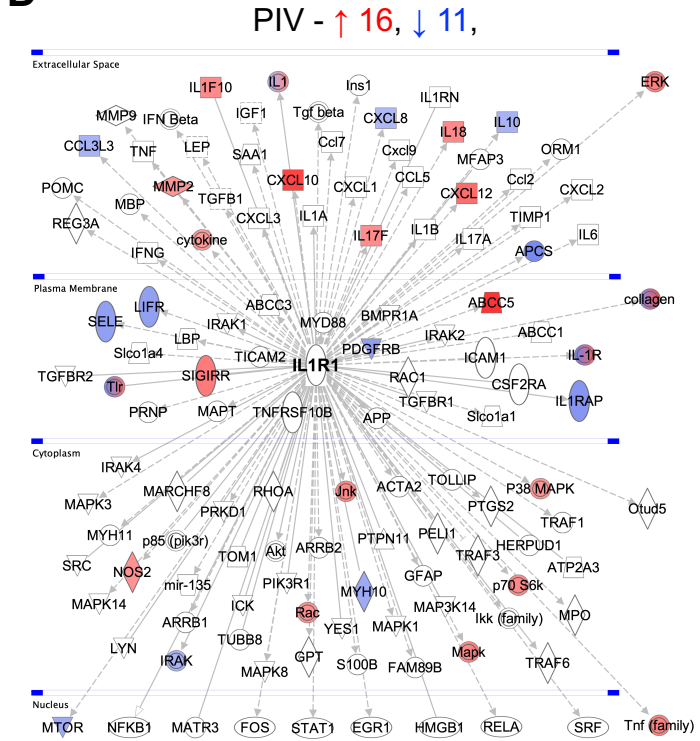
C



B



D



PV - $\uparrow 3$, $\downarrow 10$



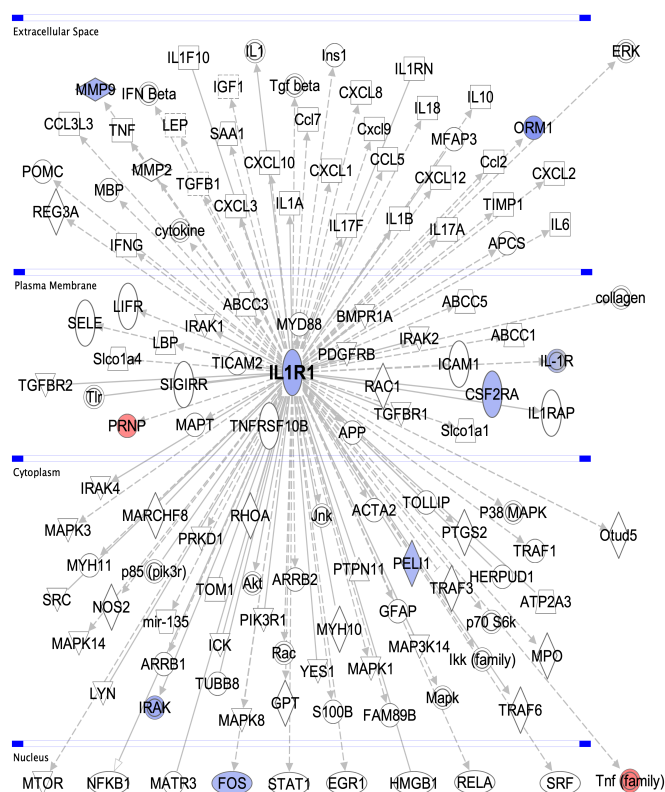
PVI- \uparrow 15, \downarrow 15, \downarrow 3



PVII - $\uparrow 4$, $\downarrow 10$



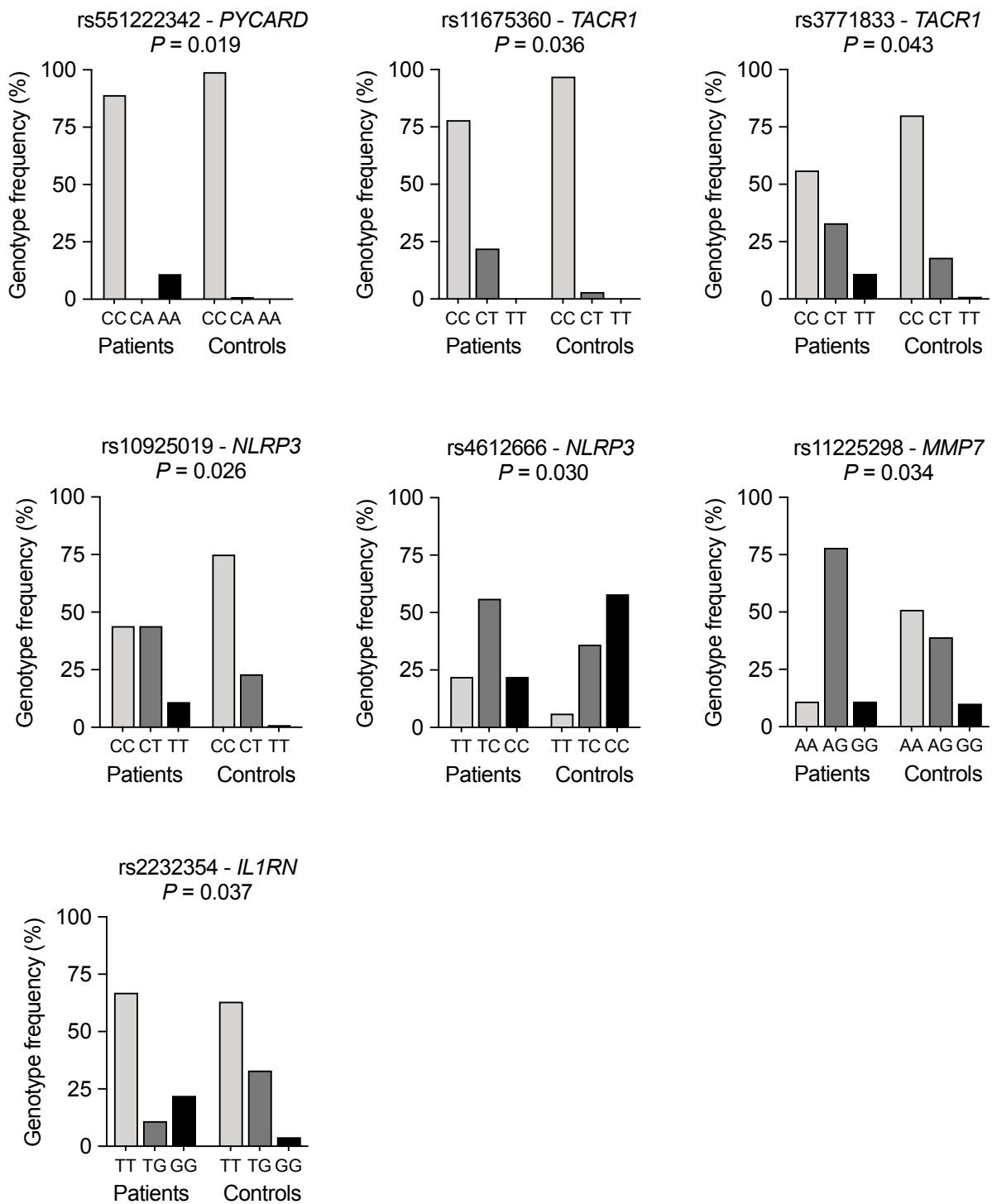
PVIII - $\uparrow 2$, $\downarrow 8$



[illegible][illegible]

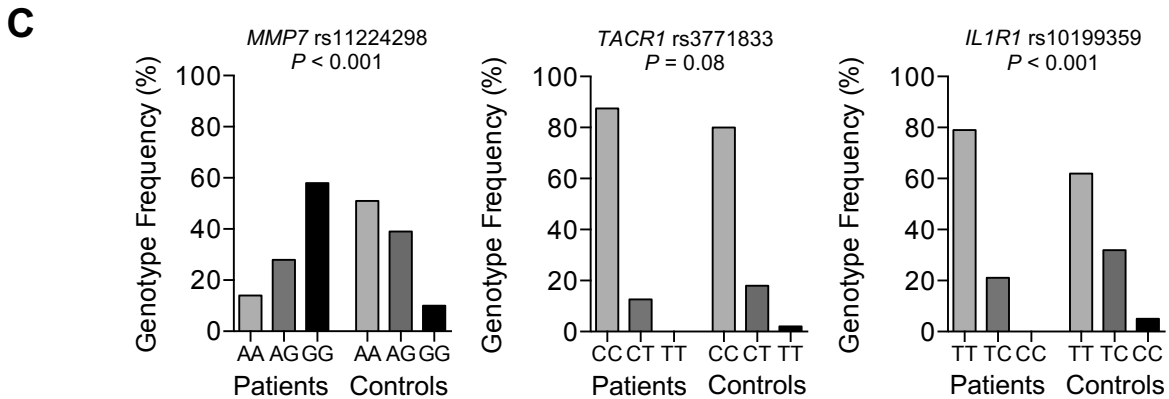
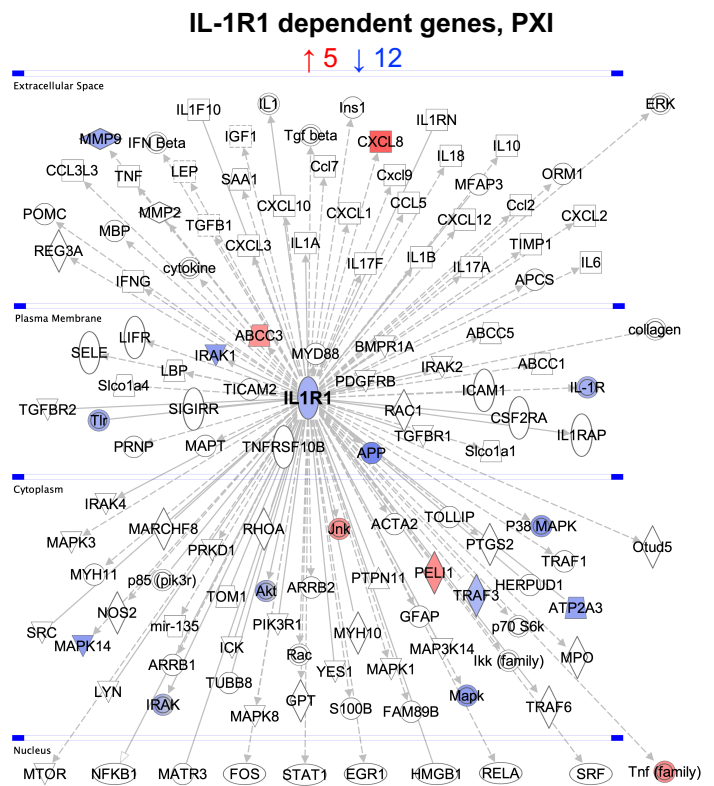
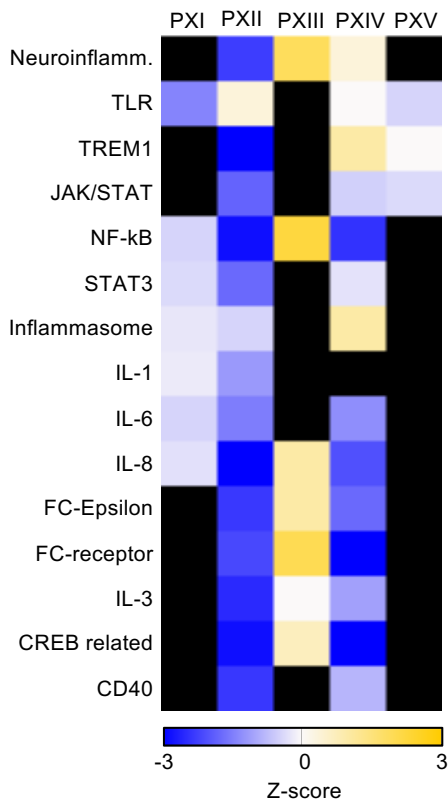
A, Heatmap comparing the post-treatment (7 days) to pre-treatment samples in individual patients (cut-off FC>1.5). **B-J**, Networks of *IL1R1*-dependant genes, which were significantly regulated. The number of upregulated (red) or down-regulated (blue) genes is indicted by the arrows.

A, Heatmap comparing the post-treatment (7 days) to pre-treatment samples in individual patients (cut-off FC>1.5). **B-J**, Networks of *IL1R1*-dependant genes, which were significantly regulated. The number of upregulated (red) or down-regulated (blue) genes is indicted by the arrows.



Supplementary Figure 3. Supplementary data for Figure 4.

Additional significant genetic variants in patients with bladder pain syndrome are shown. Histograms show genotype frequencies of disease associated SNPs compared to the 1000 Genomes control database (European population).



Gene	SNP ID	Alternative allele	Patient Genotypes	Allele Frequency %		P-value
				Patients	Control	
<i>MMP7</i>	rs11225298	G	AA GG GG AG GG AG GG AG GG	67	30	<0.001
<i>TACR1</i>	rs3771833	T	CC CT CC CC CC CT CC	28	11	0.002
<i>IL1R1</i>	rs10199359	C	TC TT TC TT TT TC TT	42	22	0.002

Supplementary Figure 4. Transcriptomic- and genetic analysis of validation controls

A, Gene expression was examined in five patients, using paired samples from day 0 and day 7. The expression of neuro-inflammatory- and IL-1-related genes was inhibited after seven days in responders from whom paired samples were available ($n=3$). Furthermore, inflammasome-, IL-6-, IL-8- and STAT3 pathway genes were inhibited. In one of the responders, neuroinflammation was weakly activated. No change was seen in the non-responder from whom paired samples were available. **B**, Pyrosequencing identified *IL1R1* and *MMP7* polymorphisms also in the second group of patients. *TACR1* or *IL1RN* variants were not detected.